REMARKS

Applicant has cancelled the nonelected claims 1-27 and 30-38 as required under 37 CFR §1.144. Applicant has amended Claim 28 and added new Claims 39, 40, 41 and 42. Support for these new Claims can be found in the Specification on page 30.

Objection

The Examiner has objected to Claim 28, because the term "prostate-derived" cell is not clear. Claim 28 has been amended to refer to a "prostate cell". Applicant believes this addresses the Examiner's objection .

Rejection under 35 U.S.C. §112

In the latest Office Action, the Examiner has basically repeated her contention that because the state of the art in this technical field is so highly unpredictable, the Specification is not enabling for the claimed invention. The Examiner states (page 4) "although there were many examples of immunoconjugates ...being used to selectively kill cells, these examples are not applicable to the claimed invention, because different antibodies behave *in vivo* differently, and one cannot predict that the PROST 03 immunoconjugate...could be used successfully *in vivo* for killing prostate cancer cells or for treating prostate cancer".

The Applicants have demonstrated the following:

(1) **PROST 03 is a prostate-specific target**. In the Specification (Example 5, pg 43, and Figure 5), Applicants have demonstrated that PROST 03 is significantly expressed only in prostate tissue (normal and tumor), with over-expression in prostate tumor, and would, therefore, be a good choice for prostate-targeted immunotherapy. The treatment of choice for localized prostate cancer is surgery or radiation. Once prostate cancer has metastasized, which often occurs relatively early in the course of the disease, there are no cures and the treatment of advanced prostate cancer focuses on the elimination of metastatic cells. "To achieve effective anti-metastatic activity against

disseminated lesions will required either systemic delivery or **localized delivery of an agent** .....Therapy with specific antibodies also has great potential and is being used clinically as an adjuvant in several cancers (Timme et al. (2003) *Currrent Drug Targets* 4:251-261, pg 252). An antibody, such as those described in the instant application, targeted to a protein whose expression is basically limited to prostate tissue, represents a therapeutic agent with great potential for the treatment of metastatic prostate disease.

(2) **PROST 03 is a cell-surface protein**. PROST 03 shows strong sequence homology to a family of sugar/proton transporter proteins, which are known to be cell-surface proteins (see Specification, pages 3 and 14). An antibody, such as those descirbed in the instant application, which is directed to a prostate-specific protein, and **wherein that protein is on the cell surface**, represents a therapeutic agent with great potential for the treatment of metastatic prostate disease.

(3) **Applicant has generated antibodies** to peptides derived from sequence of PROST 03, which is prostate-specificand located at the cell-surface (see Specification, Example 4) and **has shown that such antibodies stain prostate tumor tissue and prostate metastases** (see Specification, Example 5 and Figure 6). The technology to produce other forms of antibodies (e.g. monoclonal, chimeric, humanized or human), which are known to have characteristics that may be preferred for therapeutic use (see Specification, pg 16), is well within the knowledge-base of one skilled in the art.

Applicants have clearly provided enough information regarding the properties of PROST 03 to lead one skilled in the art of immunotherapy to have a reasonable expectation of the successful use of immunoconjugates directed against PROST 03 for use as a therapeutic approach for prostate cancer, particularly metastatic prostate cancer.

A recent review entitled "Therapeutic Targets for Metastatic Prostate Cancer" states: "One approach to antibody therapy is to fuse antibodies to cell surface markers with cytotoxic agents. Several clinical trials are underway using this approach such as radiolabeled antibody, j591, to prostate specific membrane antigen or SGN-15, a doxyrubicin conjugated antibody to Lewis Y antigen that is highly expressed in prostate cancer (Timme et al. (2003) *Current Drug Targets* 4:251-261).

The Examiner has not meet her burden in providing any information which would make one skilled in the art doubt that PROST 03 might be an equally useful therapeutic target, but has merely brought up various issues that one skilled in the art would always encounter in the normal process of preclinical drug evaluation. There is some unpredictability in any drug discovery process, but Applicants have demonstrated a tissue-specific target, the presence of that target on the cell surface, the ability of antibodies generated against the target to stain both the tissue itself *and* cells of that tissue type found as metastasis.

One skilled in the art would be convinced of the utility of such antibodies conjugated to therapeutic agents as a potential therapeutic modality for prostate cancer.

Conclusion:

Applicants respectfully submit that with the submission of the newly amended Claims 28 and addition of new Claims 39-42, the arguments presented above, the rejection of Claims 28 and 29 should be withdrawn and that the Claims are in condition for allowance.

Respectfully submitted,

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